UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,248	05/11/2001	Michael Salgaller	020093-000810US	7931

20350 7590 03/30/2006

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 03/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/854,248	SALGALLER ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/24/05, 9/29/05, and 2/13/06*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,12-14,16-21 and 36-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,12-14,16-21 and 36-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 8/24/05 and 2/13/06, and IDS, filed 9/29/06, are acknowledged.

2. Claims 10, 12-14, 16-21, and 36-43 are pending and being acted upon.

3. In view of Applicant's new showing of support, the previous rejection of Claim 36 under the first paragraph of 35 U.S.C. 112 for the introduction of new matter into the claims has been withdrawn.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 10, 12-14, 16-21, and 36-43 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,788,963 (1998, IDS) in view of Thurnher et al. (1997, IDS) and Ramoner et al. (1998, IDS).

As set forth previously, The '963 patent teaches a method for producing an anti-tumor cell, antigen specific cytotoxic T cell (CTL) response comprising administering to a patient an effective amount of human DCs, said DCs having been exposed *in vitro* to the prostate tumor associated antigenic fragment PSM-P1 (SEQ ID NO:1) derived from various sources including tumor cell lysates and purified antigens (see particularly column 8, PROSTATE SPECIFIC ANTIGENS FOR PRESENTATION BY DC). The reference further teaches that the DCs are obtained from peripheral blood, have been cryopreserved, have been obtained from a healthy HLA matched donor, are extended life span, and can be administered to a metastatic prostate cancer patient (see particularly the Claims).

The reference teaching differs from the claimed invention only in that it does not teach the use of BCG in the *in vitro* exposure of the DCs to antigen.

Thurnher et al. teaches the *in vitro* maturation and activation of DCs with BCG (see particularly pages 129-130, RESULTS, *BCG mycobacteria induce maturation of DCs*). The reference further teaches that DCs matured in the presence of BCG may also take up tumor antigens and thus, then be capable of activating tumor-reactive T cells in a cytokine milieu that favors the generation of a strong anti-tumor CTL response (see particularly page 131, DISCUSSION). The reference concludes by teaching tumor-antigen loading of DCs cultured in BCG (see particularly page 133, column 2).

Ramoner et al. further extends the work of Thurnher et al. The reference teaches that BCG "is a potent activator of human DCs." The reference further teaches that BCG stimulates the ability of DCs to activate T cells. The reference further teaches that BCG could be used in DC based tumor immunotherapy (see particularly page 1491, CONCLUSIONS).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method for producing an anti-tumor cell, antigen specific CTL response comprising administering to a patient an effective amount of human DCs, said DCs having been exposed *in vitro* to the prostate tumor associated antigenic fragment PSM-P1 (SEQ ID NO:1), said DCs having been obtained from peripheral blood, having been cryopreserved, having been obtained from a healthy HLA matched donor, having been extended life span, and having been administered to a metastatic prostate cancer patient, as taught by the '963 patent. One of ordinary skill in the art would have been motivated to add BCG to the *in vitro* exposure of DCs to antigen for an improved anti-tumor, antigen specific CTL response, given the combined teachings of Thurnher et al. and Ramoner et al. that: 1) BCG causes the maturation of DC and thus, the DCs are then capable of activating tumor-reactive T cells in a cytokine milieu that favors the generation of a strong anti-tumor CTL response and 2) BCG "is a potent activator of human DCs", BCG stimulates the ability of DCs to activate T cells, and BCG could be used in DC based tumor immunotherapy. Regarding Claims 36 and 40, said claims comprise only the routine optimization of the claimed method and fall well within the purview of one of ordinary skill in the art at the time of the invention.

Applicant's arguments, filed 2/13/06, have been fully considered but they are not persuasive. Applicant argues that the Examiner has not made a proper showing of motivation.

It remains the Examiner's position that the improved anti-tumor, antigen-specific CTL response obtainable with the combined method establishes proper motivation to combine the references. Applicant is again reminded that the characterization of how the improved immune response is achieved, i.e., through enhanced MHC Class I presentation, does not render the method of the instant claims patentably distinct.

In the remarks of 8/24/05, Applicant argues, "Peptides would not be considered an antigen that requires processing by the dendritic cell prior to presentation. Claims 14, 39 and 43 have been amended to delete the recitation of PSMA peptides".

This seems a curious argument given that the PSMA peptide of SEQ ID NO:1 is the elected species? Regardless, it remains the Examiner's position that the method of the combined references renders the method of the instant claims obvious by whatever mechanism it functions through.

Applicant argues, "Applicants do not believe that Thurnher et al disclose *in vitro* exposure of DCs to BCG provides a cytokine milieu that favors the generation of a strong anti-tumor CTL response".

The reference teaches that *in vitro* culture of DCs with BCG, among other things, enhances expression of both CD83 and CD86 expression (DC maturation markers). CD86, in particular, comprises a costimulatory molecule that would enhance the CTL response. For that reason alone it would be obvious to combine the methods of the '963 patent and Thurnher et al.

Applicant argues that the methods of Claims 36 and 40 do not comprise merely routine optimization in view of the disclosure at page 32, lines 18-29 of the specification.

At page 32, line 18, the specification discloses, "Inciting a potent anti-tumor response using immunotherapy has been limited in efficacy partly due to difficulty in stimulating a cytotoxic T cell response". It is the Examiner's position that this is precisely the reason for combining the methods of the prior art and optimizing the timing of the combined method.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 40-43 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the generic method of Claim 40 comprising

contacting antigen with DCs subsequent to contact of DCs with BCG.

Applicant again indicates that support for Claim 40 can be found in Example 2. As set forth previously, the support Applicant has indicated is not disclosed in a generic context as claimed. The specific experiments employ specific parameters, e.g., specific concentrations of reagents, and specific antigens, etc. Such disclosures provide insufficient support for the generic methods of the claims.

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

11. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-

free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

3/27/06

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600